

Application No.: 09/937,620
Amendment Dated 1 November 2004
Reply to Office Action of 9 August 2004

AMENDMENTS TO THE CLAIMS

This Listing of Claims will replace all prior versions, including listings, of claims in the application.

Listing of Claims

Claim 1 (currently amended): A method for the assessment of bone fragility and fracture risk, or osteoporosis, in a person, comprising the steps of

a) measuring the concentration of gamma-carboxylated osteocalcin (COC) in the presence of EDTA by means of at least one monoclonal or polyclonal antibody or fragment thereof, said antibody or fragment

i) is specific for gamma-carboxylated osteocalcin,

ii) recognizes either an epitope occurring in the region of the amino acids 17-24 of the gamma-carboxylated osteocalcin molecule or the tertiary structure associated with the gamma-carboxylated osteocalcin, and

iii) has specificity for gamma-carboxylated osteocalcin that is dependent on the presence of bivalent metal ions, said specificity decreasing in the presence of said metal ions; and optionally also measuring the concentration of intact osteocalcin (IOC) or total osteocalcin (TOC) in a body fluid sample of said person and determining the ratio of COC to IOC (COC/IOC ratio) or the ratio of COC to TOC (COC/TOC ratio), and

b) comparing

i) the concentration of gamma-carboxylated osteocalcin (COC) so obtained for said person to the mean concentration of gamma-carboxylated osteocalcin (mean COC) in similar body fluid samples of the population of the same age and sex, or

ii) the determined ratio COC/IOC ratio or COC/TOC ratio for said person to the mean ratio COC/IOC ratio or mean ratio COC/TOC ratio, (mean ratio COC/IOC or mean ratio COC/TOC)

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determined from measurements in similar body fluid samples of the population of the same age and sex, and

c) using whereby

- i) a measured COC for said person that is lower than the mean COC ~~as is an~~ indication of osteoporosis, bone fragility or increased risk of bone fracture in said person, or
- ii) the determined ratio a COC/IOC ratio or a COC/TOC ratio for said person that is lower than the mean ~~ratio~~ COC/IOC ~~ratio~~ or mean ~~ratio~~ COC/TOC ~~ratio is an~~ ~~as~~ indication of osteoporosis, bone fragility or increased risk of bone fracture in said person.

Claim 2 (original): The method according to claim 1 wherein the body fluid sample is a serum, plasma or urine sample.

Claim 3 (canceled).

Claim 4 (currently amended): The method according to claim 3 1 wherein COC is measured by means of one monoclonal antibody or fragment thereof, or a mixture of several monoclonal antibodies or fragments thereof recognizing any one of the epitopes specific for gamma-carboxylated osteocalcin.

Claims 5-7 (canceled).

Claim 8 (currently amended): The method according to claim 3 1 wherein the antibody fragment is a recombinantly or proteolytically produced antibody fragment.

Claim 9 (currently amended): A kit for the assessment of bone fragility and bone fracture risk, or osteoporosis in a person, comprising (a) EDTA, (b) a first capture reagent consisting of at least one monoclonal or polyclonal antibody or fragment thereof, said antibody or fragment

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i) is being specific for gamma-carboxylated osteocalcin in a body fluid sample of said person,
ii) recognizes either an epitope occurring in the region of the amino acids 17-24 of the
gamma-carboxylated osteocalcin molecule or the tertiary structure associated with the gamma-
carboxylated osteocalcin, and
iii) has specificity for gamma-carboxylated osteocalcin that is dependent on the presence of
bivalent metal ions, said specificity decreasing in the presence of said metal ions,
and (c) a detecting reagent, capable of detecting the complex formed between the capture reagent
and the antigen gamma-carboxylated osteocalcin.

Claim 10 (currently amended): The kit according to claim 9 comprising further another a
second capture reagent consisting of at least one monoclonal or polyclonal antibody or fragment
thereof, said antibody or fragment being able to capture any osteocalcin (intact OC; total OC) in a
body fluid sample of a person, and a second detecting reagent, capable of detecting the a complex
formed between the second capture reagent and the antigen any osteocalcin.

Claim 11 (currently amended): The kit according to claim 9 wherein the first capture reagent
is one monoclonal antibody or fragment thereof, or a mixture of several monoclonal antibodies or
fragments thereof recognizing any one of the epitopes specific for gamma-carboxylated osteocalcin.

Claims 12-14 (canceled).

Claim 15 (previously presented): The kit according to claim 9 wherein the capture antibody
fragment is a recombinantly or proteolytically produced antibody fragment.

Claim 16 (canceled).

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Claim 17 (currently amended): The method according to claim ~~16~~ 2 wherein COC is measured by means of one monoclonal antibody or fragment thereof, or a mixture of several monoclonal antibodies or fragments thereof recognizing any one of the epitopes specific for gamma-carboxylated osteocalcin.

Claims 18-20 (canceled).

Claim 21 (new): The method according to claim 2 wherein the antibody fragment is a recombinantly or proteolytically produced antibody fragment.

Claim 22 (new): The method according to claim 4 wherein the antibody fragment is a recombinantly or proteolytically produced antibody fragment.

Claim 23 (new): The method according to claim 17 wherein the antibody fragment is a recombinantly or proteolytically produced antibody fragment.

Claim 24 (new): The kit according to claim 10 wherein the first capture reagent is one monoclonal antibody or fragment thereof, or a mixture of several monoclonal antibodies or fragments thereof recognizing any one of the epitopes specific for gamma-carboxylated osteocalcin.

Claim 25 (new): The kit according to claim 10 wherein the first capture antibody fragment is a recombinantly or proteolytically produced antibody fragment.

Claim 26 (new): The kit according to claim 15 wherein the first capture antibody fragment is a recombinantly or proteolytically produced antibody fragment.

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Claim 27 (new): The kit according to claim 24 wherein the first capture antibody fragment is a recombinantly or proteolytically produced antibody fragment.